

needed to sort, separate, order, and focus particles of a predetermined size or particles of multiple predetermined sizes.

[0143] The channels used in the systems described herein can have various geometries and cross-sections for focusing particles of a predetermined size suspended within a fluid. For example, in one embodiment illustrated in FIGS. 2A and 2B, a straight channel 30 is provided having a rectangular cross-section with an aspect ratio of substantially 1 to 1. As will be described in more detail below, particles of a predetermined size flowing within such a channel geometry will be separated, ordered, and focused into four streamlines 32a, 32b, 32c, 32d corresponding to four equilibrium points or potential minimums at a distance from each face of the four channel walls. In another embodiment, a straight channel 36 is provided having a rectangular cross-section with an aspect ratio of substantially 2 to 1. Particles of a predetermined size flowing within such a channel geometry can be separated, ordered, and focused into two focused streamlines 38a, 38b corresponding to two equilibrium points or potential minimums along top and bottom walls across the width of the channel. In one embodiment, an aspect ratio of 1 to 2 can also be used.

[0144] The channels may also be curved as shown in FIGS. 3A and 3B. For example, symmetrically curved channels can be provided such as S-shaped, sinusoidal, or sigmoidal shaped channel 40 having a rectangular cross-section. Particles of a predetermined size flowing within such a channel geometry will be generally focused into two streamlines 42a, 42b corresponding to two equilibrium points or potential minimums at a distance from left and right side faces of the channel. An aspect ratio of a sigmoidal channel 40 can be substantially 1 to 1 and/or can vary along a length thereof. For example, the aspect ratio of a sigmoidal channel can vary over the length of the channel between 1 to 1 and 2 to 1 depending on the configuration chosen.

[0145] In another embodiment, asymmetrically curved channels are provided as shown in FIGS. 4A and 4B. While asymmetrically curved channels can have various shapes and configurations as needed for a particular application, in one embodiment an asymmetric channel 46 can generally have the shape of a wave having large and small turns, where a radius of curvature can change after each inflection point of the wave. Each large and small turn can have a specified width of the channel associated with the turn. In particular as shown in FIG. 4A, one-half of a wavelength of the wave can have a large curve with a radius R_{1a} , R_{1b} defining a width W_1 . A second half of the wavelength can have a curve with a radius R_{2a} , R_{2b} defining a width W_2 , where R_{1a} and R_{1b} can be greater than R_{2a} and R_{2b} , and vice versa (and where $R_{1a}=R_{2a}$ and $R_{1b}=R_{2b}$ would be a sinusoidal, symmetric shaped channel as indicated above). In addition, W_1 can be greater than W_2 , and vice versa. The wavelength having a first half with the radius R_{1a} , R_{1b} and the second half with the radius R_{2a} , R_{2b} can then be repeated as many times as needed, varying after each inflection point, to provide a specified length of channel with an asymmetric curve. The asymmetrically curved channel 46 can also have a rectangular cross-section with an aspect ratio that can vary as needed over the channel length depending on the nature of the asymmetry in the curves. In one embodiment, the aspect ratio can vary between 1 to 1 and 2 to 1. In this case, a single focused stream 48 of particles is created corresponding to a single equilibrium point or potential minimum within the channel 46. In other embodiments, asymmetric curving channels, in particular an

expanding spiral shaped channel 50 can be provided as shown in FIG. 4C, having a rectangular cross-section with an aspect ratio of substantially 2 to 1, although the aspect ratio can vary. In this case, particles are focused into a single stream line a distance away from an inner wall of the channel corresponding to a single equilibrium point or potential minimum within the channel.

[0146] Aspect ratios of all channels described above and herein, including straight, symmetric, and asymmetric, can vary as needed from one application to another and/or as many times as needed over the course of a channel. In embodiments illustrated in FIG. 4, aspect ratios are shown as 1 to 1 and 2 to 1, however, a person of ordinary skill will recognize that a variety of aspect ratios could be employed. In addition, the choice of width to height as the standard for determining the aspect ratio is somewhat arbitrary in that the aspect ratio can be taken to be the ratio of a first cross-sectional channel dimension to a second cross-sectional channel dimension, and for rectangular channels this would be either width to height or height to width. By way of further example, the aspect ratio of the channel of FIG. 4C could be expressed as either 2 to 1 or 1 to 2, as could the aspect ratio of the channel illustrated in FIG. 9A in which the height is twice the width.

[0147] Other channel cross-sections can also be included in each of the geometries noted above. Channel cross-sections can include, but are not limited to, circular, triangular, diamond, and hemispherical. Particles of a predetermined size can be focused in each of these exemplary cross-sections, and the equilibrium positions will be dependent on the geometry of the channel. For example, in a straight channel having a circular or hemispherical cross-section, an annulus or arc of focused particles can be formed within the channel. In a straight channel having a triangular or diamond cross-section, particles can be focused into streamlines corresponding to equilibrium positions at a distance from the flat faces of each wall in the geometry. As symmetric and asymmetric curving channels are included having each of the exemplary cross-sections noted above, focusing streams and equilibrium positions can generally correspond to that described above with respect to the channels having a rectangular cross-section.

[0148] In general, there are certain parameters within straight, symmetric, and asymmetric microfluidic channels which lead to optimal ordering and focusing conditions for particles suspended within a sample. These parameters can include, for example, channel geometries, particle size with respect to channel geometries, properties of fluid flow through microfluidic channels, and forces associated with particles flowing within microfluidic channels under laminar flow conditions. It is presently believed that the forces acting on the particles can be referred to as inertial forces, however, it is possible that other forces contribute to the focusing and ordering behaviors. Exemplary inertial forces can include, but are not limited to, inertial lift down shear gradients and away from channel walls, Dean drag (viscous drag), pressure drag from Dean flow, and centrifugal forces acting on individual particles. FIGS. 5A-7 will be used to illustrate concepts associated with these parameters in the theory described below, with FIGS. 5A-5B generally referring to parameters associated with straight channels and FIGS. 6A-7 referring to parameters associated with curving channels. The theory discussed below is meant to be solely descriptive and exemplary and, while the behavior of systems designed using these principles can be predicted using this theory, the theory presented